II. Remarks

A. The Provisional Rejection Under The Judicially Created Doctrine of Obviousness-Type Double Patenting Should Be Withdrawn

Claims 32-41 and 43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 09/726,650. The Examiner is invited to note that claim 1 of copending Application No. 09/726,650 is cancelled. Therefore, the applicants respectfully submit that the provisional rejection under the judicially created doctrine of obviousness-type double patenting over claim 1 of copending Application No. 09/726,650 should be withdrawn.

B. The Rejection Under 35 U.S.C. § 102(b) Should Be Withdrawn

Claims 32-41 and 43 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Tramontano (U.S. Patent No. 4,659,567, "Tramontano"). The rejection should be withdrawn because the reference fails to teach every limitation of the present claims. The applicants respectfully submit that the Examiner is ignoring explicit limitations of the instant claims. When the instant claims are properly viewed in their entirety, including all of the recited limitations, the applicants submit that the claims are novel over the art referred to by the Examiner because the art does not teach each and every element of the present claim as is required under the law to properly anticipate an invention.

The Examiner has characterized the instant claims as being "drawn to antibodies, more narrowly recited as catalytic antibodies, made by the recited process." The Examiner has characterized Tramontano as teaching "antibodies which catalyze chemical reactions." However, Tramontano teaches the production of antibodies raised in an animal and by

hybridoma technology. The present invention is concerned with a catalytic antibody produced by a synthetic method in which a genetic library is generated and represents the immune repertoire of an animal. More specifically, the present invention provides an antibody such as a catalytic antibody by a method in which a large number of different antibody variable region genes (i.e., V_L and V_H) is cloned and expressed in expression vectors. The inventors described and used a set of DNA primers which are capable of hybridizing to a much larger number of antibody genes allowing amplification of these genes using PCR which results in a genetically diverse population of V_H or V_L coding sequences.

The Examiner also alleges that it is not clear how to interpret claims 38-41 of the instant invention stating that the meaning of the phrase "are not encoded together in the genome of a single naturally occurring cell" is unclear and could be read to encompass Tramontano. The applicants submit that this rejection is moot in view of the fact that claims 40 and 41 have been cancelled and claim 38 has been amended to eliminate the language at issue and to point out specifically that V_H and V_L encoding sequences are carried by a prokaryotic replicon.

In summary, since no piece of any prior art discloses all of the elements claimed in the instant invention, the applicants respectfully submit that the rejection under 35 U.S.C. § 102(b) is improper and should be reconsidered and withdrawn.

C. The Rejection Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

The Examiner rejected claims 32-41 and 43 under 35 U.S.C. 112, first paragraph, alleging inadequate written description of the claimed invention. According to the Examiner, "the claimed invention is drawn to a very broad genus, i.e., catalytic antibodies. Applicants have not conveyed to one of skill at the time of filing that they, Applicants, were in possession of the full scope of the claimed invention."

The present claims are directed to antibodies such as catalytic antibodies made by the recited process. The architecture of antibody structure is well known in the art. Figure 1 of the instant application illustrates the principal structural features of an antibody. More detailed structural features of the variable regions of antibody light and heavy chains are illustrated in Figure 2. The description at page 19 lines 22-31 provides further detail as to the general size of these regions. The skilled person will be familiar with the overall principal structural features of an antibody.

The specific structure of any of the antibodies generated by the recited method was not known *a priori* and this did not prevent the applicants from generating and identifying any of the antibodies. In fact, it is common practice in the field of the antibody production to generate an antibody without knowing its specific structure *a priori*, particularly in view of the fact that the specific structure is understood to be in the context of the overall general structure known and well understood by those of skill in the art. Furthermore, it is common practice in the field of antibody production to characterise an antibody by its ability to bind a particular target (antigen). The Examiner is invited to note three major points of the argument: 1) *a priori* knowledge of the specific structure of an antibody is not required to practice the instant invention; 2) since a catalytic antibody is a species of the genus "antibody", the applicants had the invention in their possession at the time of filing; and 3) the catalytic antibodies of the present invention are defined by their selective and specific binding to targets chosen by an artisan practicing the invention.

The applicants have demonstrated that a library produced by the claimed process contains antibodies that bind a particular transition state hapten (NPN). (See, *e.g.*, Figure 13 described in detail at page 10, lines 9-18, and Example 18, particularly 18C, and pages 84-85 of the specification which were subsequently shown to have the predicted catalytic activity)

(See Sastry *et al.*, *Catalytic Antibodies*, 1991, Ciba Foundation, 159, pp. 145-155 (Exhibit A) of which one of the authors is an inventor of the presently claimed subject matter.)

Thus, the method of the present invention eliminates any need for the kind of structure-function information discussed by the Examiner other than the fact that the polypeptides are V_H and V_L polypeptides which are provided by the described methods and which in combination have catalytic activity. If in fact structure-function information becomes desirable, one could obtain an antibody, which binds to a target, and has a catalytic activity using the methods of the present invention and then analyze the structure of the antibody so obtained to ascertain any structure-function relationship that might be desired. However, such information is demonstrably unnecessary to practice the presently claimed invention.

Furthermore, there are many cases when the U.S. Patent Office has granted genetic claims for antibodies to novel targets with no requirement that the detailed structure of the antibody to such a target is described. For example, U.S. patents 6,548,641; 6,545,130; 6,545,128 and 6,521,228 (attached as Exhibits B, C, D and E) claim antibodies without any description of structural features of the antibodies. Rather, the antibodies are defined by reference to the type of target they act upon and not by reference to any structural feature. The Examiner is invited to note especially that claim 28 of U.S. patent 6,521,228 claims not only an antibody which binds a target but also exerts a functional effect in doing so. There is no requirement under U.S. law to define the specific structural features of an antibody when those of skill in the art are capable of generating any number of antibodies which can differ in their precise structure, but all of which have the overall gross structural features of an antibody and the additional feature of binding a particular defined class of targets. Still further, the claims of the present application provide more structural information than the

claims of the cited patents: by virtue of its recitation of a V_H and V_L polypeptide which in combination have a catalytic activity.

In view of the foregoing arguments, the applicants respectfully submit that the rejection under 35 U.S.C. § 112, first paragraph, is improper and should be withdrawn.

With respect to claims 38-41, the Examiner alleges that since "it would be impossible to have known all co-existing V_H and V_L sequences even in just one species, the [instant] specification could not have provided a fully meaningful or useful description of the invention with respect to this limitation." Claim 38 is amended to incorporate a distinct feature of the instant invention, specifically to point out that V_H and V_L encoding sequences are carried by a prokaryotic replicon. Claims 40 and 41 are cancelled.

The applicants respectfully submit that knowledge of all co-existing V_H and V_L sequences is not necessary to practice the instant invention as defined by amended claim 38. The written description teaches in detail how to make genetic libraries from different cell types. A person skilled in the art is enabled by the written description to make V_H library and V_L library from any cells containing genes coding for the V_H and/or V_L polypeptides chosen by an artisan practicing the instant invention and then to screen for a catalytic antibody comprising V_L and V_H polypeptides against an antigen of his/her choice.

In view of the foregoing arguments, the applicants respectfully submit that the written description of the instant invention both: 1) clearly demonstrates that the applicants had the instant invention in their possession at the time of filing of the instant application; and 2) fully enables a person skilled in the art to practice the instant invention. Therefore, the applicants respectfully submit that the rejections under 35 U.S.C. § 112, first paragraph, should be withdrawn.

C. The Rejection Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

The Examiner has rejected claims 38-41 and 43 as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Examiner alleges that the limitation to V_H and V_L domains not encoded together in the genome of a single naturally occurring cell is not definite because "it would not have been possible for anyone to know all of the combinations of heavy and light antibody chains in every human being in existence, let alone in all species that possess antibodies." The applicants respectfully submit that the rejection is moot in view of the foregoing claim cancellation and the amendment to claim 38 which has been amended to eliminate the limitation to V_H and V_L domains not encoded together in the genome of a single naturally occurring cell and to point out specifically that V_H and V_L encoding sequences are carried by a prokaryotic replicon. The applicants respectfully submit that claim 38, as currently amended, specifically points out and distinctly claims the subject matter which applicants regard as the invention and therefore the rejection should be withdrawn.

As regards claim 43 depending upon a cancelled claim, the claim has been rewritten in an independent form and therefore the rejection should be withdrawn.

The applicants respectfully submit that the instant claims particularly point out and distinctly claim the subject matter which the applicants regard as the invention. In view of the foregoing amendments and arguments, the applicants request that the rejection under 35 U.S.C. § 112, second paragraph, should be withdrawn.

Conclusion

The applicants submit that claims 32-39 and 43 are in condition for allowance and early notification thereof is solicited. The Commissioner is hereby authorized to charge any fees that may be required in the Application to Deposit Account No. 54-1214.

Respectfully submitted,

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